

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
11 December 2003 (11.12.2003)

PCT

(10) International Publication Number
WO 2003/101996 A3

(51) International Patent Classification⁷: **C07D 491/22**,
A61K 31/4375, A61P 35/00, 31/12, 33/00

30400, I-00040 Pomezia (IT). ZUNINO, Franco [IT/IT];
Istituto Nazionale per lo Studio e la Cura dei Tumori, Via
Venezian, 1, I-20133 Milano (IT).

(21) International Application Number:
PCT/IT2003/000329

(74) Agent: SPADARO, Marco et al.; Cavattoni-Raimondi,
Viale dei Parioli, 160, I-00197 Roma (IT).

(22) International Filing Date: 28 May 2003 (28.05.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
RM2002A000306 31 May 2002 (31.05.2002) IT

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD,
SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US,
UZ, VC, VN, YU, ZA, ZM, ZW.

(71) Applicants (*for all designated States except US*):
SIGMA-TAU INDUSTRIE FARMACEUTICHE RI-
UNITE S.p.A [IT/IT]; Viale Shakespeare, 47, I-00144
Roma (IT). ISTITUTO NAZIONALE PER LO STU-
DIO E LA CURA DEI TUMORI [IT/IT]; Via Venezian,
1, I-20133 Milano (IT).

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): MARZI, Mauro
[IT/IT]; Sigma-Tau Industrie Farmaceutiche Riunite
S.p.A., Via Pontina, Km 30400, I-00040 Pomezia (IT).
ALLOATTI, Domenico [IT/IT]; Sigma-Tau Industrie
Farmaceutiche Riunite S.p.A., Via Pontina, Km 30400,
I-00040 Pomezia (IT). PISANO, Claudio [IT/IT];
Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Via
Pontina, Km 30400, I-00040 Pomezia (IT). TINTI,
Maria, Ornella [IT/IT]; Sigma-Tau Industrie Farmaceu-
tiche Riunite S.p.A., Via Pontina, Km 30400, I-00040
Pomezia (IT). VESCI, Loredana [IT/IT]; Sigma-Tau
Industrie Farmaceutiche Riunite S.p.A., Via Pontina, Km

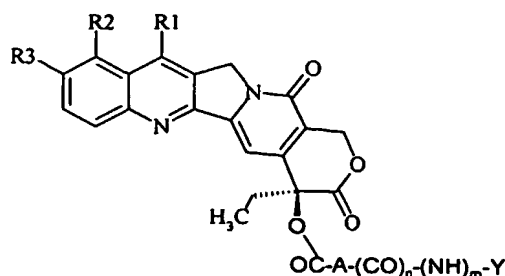
Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
29 January 2004

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: ESTERS IN POSITION 20 OF CAMPTOTHECINS



(I)

(57) Abstract: Formula (I) compounds are described:
(I) where the groups are as defined in the description
here below, the racemic mixtures, their individual
enantiomers, their individual diastereoisomers, their
mixtures, and their pharmaceutically acceptable salts.
Said compounds are topoisomerase I inhibitors.

INTERNATIONAL SEARCH REPORT

another application no.
PCT/IT 03/00329

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D491/22 A61K31/4375 A61P35/00 A61P31/12 A61P33/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 943 579 A (VISHNUVAJJALA B RAO ET AL) 24 July 1990 (1990-07-24) Abstract; claims 1-3; examples 1,2.	1,3,7,8, 11,12
Y	WO 01 49691 A (BALASUBRAMANIAN NEELAKANTAN; VYAS DOLATRAI (US); WALL MONROE E (US) 12 July 2001 (2001-07-12) Abstract; page 2, lines 25-26; claim 1, compounds (II), in particular definition of R7; and page 16, example 4: camptothecin-20-beta-Ala-Lys ester dihydrochloride.	1,2,4, 6-13
	----- -/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

29 August 2003

Date of mailing of the international search report

01.12.03

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Weisbrod, T.

INTERNATIONAL SEARCH REPORT

international application no.
PCT/IT 03/00329

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>MATSUMOTO, H. ET AL.: "Controlled Drug Release: New Water-Soluble Prodrugs of an HIV Protease Inhibitor" BIOORG. MED. CHEM. LETT., vol. 11, 2001, pages 605-609, XP002252920 cited in the application Page 605, last paragraph; page 606, figure 1; page 607, table 1.</p> <p>-----</p>	<p>1,2,4, 6-13</p>

INTERNATIONAL SEARCH REPORT

PCT/IT 03/00329

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1, 4, 7-13 (all part); 2 and 6 (complete)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1, 4, 7-13 (all part); 2 and 6 (complete)

directed to compounds (I) wherein $n = m = 1$, as well as
subject matter referring to such compounds (I).

2. claims: 1, 4, 7-13 (all part); 3 and 5 (complete)

directed to compounds (I) wherein $n = m = 0$, as well as
subject matter referring to such compounds (I).

INTERNATIONAL SEARCH REPORT

national application no.
PCT/IT 03/00329

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 4943579	A	24-07-1990	NONE		
WO 0149691	A	12-07-2001	US	6288072 B1	11-09-2001
			AU	5453800 A	16-07-2001
			CA	2396030 A1	12-07-2001
			EP	1254141 A1	06-11-2002
			JP	2003519234 T	17-06-2003
			NO	20023175 A	29-08-2002
			WO	0149691 A1	12-07-2001